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Ion-selective electrodes based on organoboron compounds as neurotransmitter receptors

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Abstract

The objective of this work was to construct ion-selective electrodes (ISEs) based on polymer membranes containing organoboron derivatives as receptors of neurotransmitters. For this purpose, appropriate organoboron compounds were synthesized or purchased (if commercially available) and introduced into poly(vinyl chloride) plasticized membranes. The main working parameters of the developed potentiometric sensors towards selected neurotransmitters (dopamine, tauryne, acetylcholine, 2-phenylethylamine) were determined. The results allowed to estimate the suitability of the selected organoboron compounds as specific neurotransmitter receptors.

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Keywords: Ion-selective electrodes; organoboron compounds; neurotransmitters

1. Introduction

The concentration of neurotransmitters in brain correlates with neuropathologies (e.g. Parkinson's disease, schizophrenia, epilepsy, depression and Alzheimer's disease), because the neurotransmitters are involved in many brain processes. Currently the causes of these diseases are not found and there are no efficient methods for their treatment. Research on the development of drugs for treatment or to delay the occurrence of disease is still continued. Therefore, it is very important to develop accurate methods of diagnostics, since early diagnosis of Parkinson's or Alzheimer's disease can improve the quality of life of patients.

At present, the determination of neurotransmitters demands expensive methods such as reverse-phase high performance liquid chromatography (HPLC) [1]. Ongoing interest in the neurotransmitters detection stimulates the

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development of cheaper and more simple analytical methods for chemical sensing of these compounds. The chemical sensors have been widely used as an alternative to the expensive chromatographic methods, because of several aspects. First of all, the cost of the analysis (i.e. the determination of the analyte) with the use of chemical sensors is relatively low. In addition, the samples do not require prior derivatization, which shortens the duration of the process. At the same time it is possible to automate the measurements and create miniaturized devices based on chemical sensors.

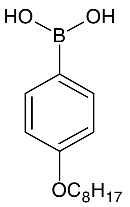
In recent years, some attempts have been made to elaborate potentiometric and voltammetric analytical methods with boronic acids and their esters as molecular receptors [2,3]. Due to the increasing interest in this field, new potentiometric sensors, based on boronic acids derivatives, were also designed for the quantitative analysis of neurotransmitters [4,5].

In this work polymer membrane ion-selective electrodes (ISEs) based on three organoboron compounds (4-octyloxyboronic acid - OPBA, 3,3'-piperazine-bis(benzoxaborol) and corresponding diboronic acid – see Figure 1) were developed. The performances of the sensors towards selected neurotransmitters were determined and compared with those measured for ion-selective electrodes containing only an ion-exchanger (KTFPB) in the membrane.

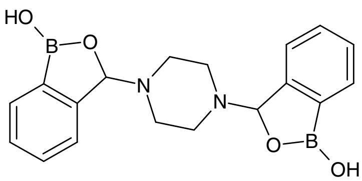
2. Experimental

The methods of the membranes and electrodes preparation/conditioning were the same as for the standard ISEs. The membranes contained 2 wt% ionophore (organoboron compound), 10 mol% versus ionophore lipophilic salt (KTFPB), 65-66 wt% plasticizer and 31-33 wt% high-molecular-weight PVC (the membranes based on an ion-exchanger contained 2 wt% KTFPB).The membrane components (200 mg in total) were dissolved in 2 ml of tetrahydrofuran (THF). This solution was poured into a glass ring placed on a glass plate leaving to evaporate the THF. Discs of suitable size was cut off from the prepared membranes and mounted in classical electrode bodies (IS 561, Philips). The constructed ISEs were preconditioned in a dilute solution of internal electrolyte for 24 hours.

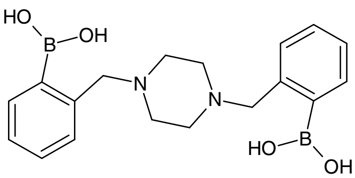
All measurements were carried out with cells of the following type: Ag, AgCl; KCl 1 M / CH_3COOLi 1 M / sample solution // membrane // internal filling solution; AgCl, Ag. Potentiometric multiplexer (EMF 16 Interface, Lawson Labs Inc., Malvern, USA) was used for the EMF measurements. The calibration curves of the electrodes towards selected neurotransmitter (in the concentration range from 10^{-6} to 10^{-2} M) were examined by measuring the EMFs in buffer solution at various pH (pH=4.5, pH=7.0 and pH=9.0). Potentiometric selectivity coefficients of the electrodes were determined by the separate solution method (SSM) in buffered solution at various pH.



OPBA



3,3'-piperazine-bis(benzoxaborol) - PBBB



Diboronic acid - DBA

Fig. 1: The structures of organoboron compounds

3. Result and discussion

The performances of the developed sensors towards four selected neurotransmitters were evaluated in buffered solutions at different pH. The electrodes constructed by incorporating the organoboron compounds within the PVC plasticized membrane were found to respond potentiometrically to the tested neurotransmitters. This effect was observed for the electrodes containing all studied organoboron receptors (see exemplary characteritics of the sensors based on DBA receptor in Figure 2). The comparison of the dopamine responses of ion-selective electrodes based on different organoboron compounds and solely KTFPB was presented in Figure 3. Unfortunately, higher sensitivity towards the tested neurotransmitters was registered for the sensors based on KTFPB lipophilic salt (but with sligthly worse detection limit).

The presence of KTFPB in the polymer membranes increased the response sensitivity as well the detection limit of the sensors (see Figure 4). The highest sensitivity was recorded for 2-phenylethylamine, whereas the values of the response slope for taurine did not exceed the level of noise. Comparable results were obtained for the electrodes containing only the organoboron receptors.

Potentiometric responses towards dopamine, acetylocholine and 2-phenylethylamine measured in various pH conditions were compared. In general, silmilar characteristics were observed in acidic and basic conditions, whereas sligthly worse sensitivity was noticed in neutral pH. An enhanced taurine response was only measured in alkaline solution, but in a quite narrow range: 10^{-3}M - 10^{-2} M.

Finally, the values of the determined selectivity coefficients indicated, that the incorporation of the organoboron receptors to the membrane did not significantly influence the selectivity of the electrodes based on KTFPB, regardless of pH conditions.

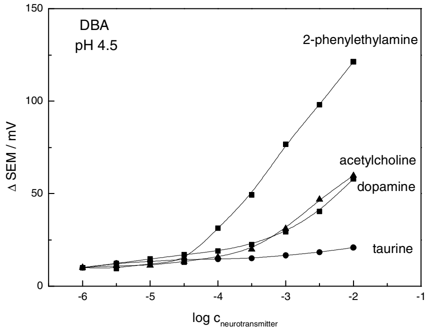


Fig. 2: The neurotransmitters responses of ion-selective electrodes based on diboronic acid measured in buffer solution at pH 4.5

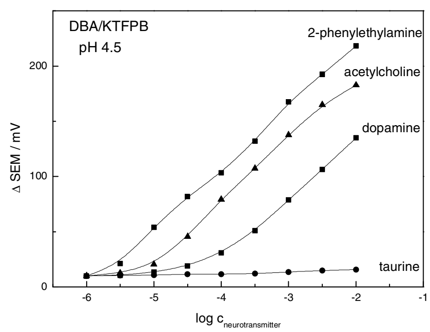


Fig. 3: The neurotransmitters responses of ion-selective electrodes based on diboronic acid with 10 mol% lipophilic salt measured in buffer solution at pH 4.5

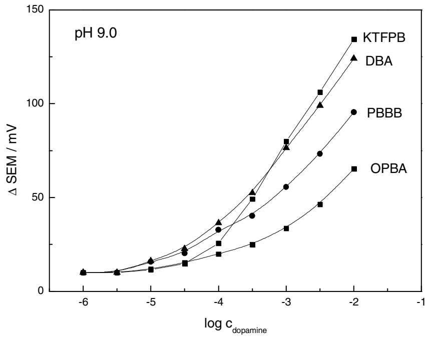


Fig. 4: The dopamine responses of ion-selective electrodes based on organoboron compounds, measured in buffer solution at pH 9.0

The results obtained showed, that the analysis of neurotransmitters can be carried out using potentiometric sensors based on the organoboron receptors. However, the introduction of the organoboron compounds to the polymeric membrane did not alter significantly the performances of the electrodes with membranes containing 10 mol% KTFPB. Therefore, further research should be focused on the synthesis of organoboron receptors providing better selectivity and sensitivity of the sensors.

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